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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/584,978	06/02/2000	Dr. Rudi Neirinckx	44334	5707

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/584,978	NEIRINCKX, DR. RUDI	
	Examin r	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication app ars on the cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-17* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 9 and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9 and in the paper filed August 28, 2003.

Applicant's election with traverse of the invention of Group II in Paper No. 9 and in the paper filed August 28, 2003 is acknowledged. The traversal is on the ground(s) that the search required for claims 9 and 10 would include the search required for Group II and therefore would not constitute an undue burden. This is not found persuasive because the search required for claims 9 and 10 is not required for Group II, e.g., would require additional searching of the FGF, urogastrone, and EGF fraction art, and would constitute an undue burden. The searches are not coextensive because the active agents in each set of claims are patentably distinct from one another.

The requirement is still deemed proper and is therefore made FINAL.

This application contains claims 9 and 10 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

2. The abstract of the disclosure filed August 28, 2003 is objected to because the Abstract is insufficiently detailed as to the possible additional ingredients (e.g. anti-inflammatory products sulfadiazine) and possible alternative ingredients (e.g., FGF and urogastrone). Correction is required. See MPEP § 608.01(b).

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. To the extent that Applicants are reciting in claims 15 and 16 that sulfadiazine is an anti-inflammatory product, claims 15 and 16 are not supported by the original disclosure of the invention, which does not recite that sulfadiazine is an anti-inflammatory product. Further, the examiner can find no recognition in the prior art that sulfadiazine has anti-inflammatory properties.

4. Claims 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 15 and 16 are unclear as to whether sulfadiazine is a species of the anti-inflammatory product required by claim 14, upon which claims 15 and 16 depend, or whether claims 15 and 16 are requiring that sulfadiazine be used in addition to the EGF required by independent claim 11 and in addition to the anti-inflammatory product required by claim 14.

5. Claims 14-16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Independent claim 11 specifies that EGF is the sole active agent of the formulation. However, dependent claims 14-16 specify additional active ingredients, i.e.

anti-inflammatory products and sulfadiazine, and therefore fall outside of the scope of the independent claim.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Much of the claimed subject matter is not recited in the specification. For example, the claimed recitations of formulations in general or of gels in particular; the concentrations recited in claims 12, 13, and 15-17; and the claimed optional additional or alternative components such as anti-inflammatory products, dermatologically-beneficial products, FGF, products with biological actions similar to EGF, urogastrone, and fractions of the EGF molecule; are not recited in the specification.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 11-13 are rejected under 35 U.S.C. 103(a) as being obvious over the Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301). The Nanney et al article teaches treating psoriasis by topically administering sufficient EGF to downregulate EGF-R. In particular, the Nanney et al article teaches creams comprising 10 and 50 μg/ml EGF. Treatment is of active human psoriatic lesions grafted onto congenital athymic nude mice. The nude mouse model of psoriasis is described as being an "excellent biological tool to investigate the in vivo implications of an exogenous (paracrine) mode of cytokine delivery." See, e.g., the Abstract; page 29, column 1, second and third full paragraphs; and page 300, column 2, first full paragraph. The Nanney et al article does not teach using its EGF compositions to treat psoriasis in human patients. It would have been obvious to one of ordinary skill in the art at the time Applicant's

invention was made to use the EGF compositions of the Nanney et a article to treat psoriasis in human patients because it is desirable to treat psoriasis in human patients, because the Nanney et al article teaches that active human psoriatic lesions can be treated with the EGF compositions, albeit grafted onto athymic nude mice, and because the mouse model is described as being an excellent biological tool and therefore would have been considered to be reasonably predictive of in vivo success in humans.

9. Claims 11-13 are rejected under 35 U.S.C. 103(a) as being obvious over the Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301) as applied against claims 11-13 above, and further in view of Njieha et al (U.S. Patent No. 5,070,188) and Cini et al (U.S. Patent No. 5,130,298). The Nanney et al article does not teach treating psoriasis in humans. Njieha et al (see especially column 1, lines 18-20, and column 5, lines 10-12) and Cini et al (see especially column 5, lines 28-34) teach that EGF-containing compositions can be used to treat psoriasis and thus constitute further evidence that the EGF compositions of the Nanney et al article would reasonably have been expected to be useful in the treatment of psoriasis in humans.

10. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being obvious over the Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301) as applied against claims 11-13 above, and further in view of the Casaco et al article (Skin Pharmacol. Appl. Skin Physiol., Vol. 12, pages 79-84). The Nanney et al article does not describe its EGF as having anti-inflammatory properties. The Casaco et al article teaches that EGF has anti-inflammatory activity. See, e.g., the Abstract; page 80, column 1, first full paragraph; and page 83, column 2. Accordingly, the EGF compositions taught by the Nanney et al article also comprise an anti-inflammatory product, namely the EGF itself. Applicants' claims do not require that the anti-inflammatory

product be different than the EGF, and in view of the "sole active agent" language, Applicants' claims may be interpreted as requiring the EGF and the anti-inflammatory product to be the same. With respect to the issue of treating psoriasis in humans with the compositions of the Nanney et al article, the Casaco et al article also describes EGF as having anti-psoriatic actions (see page 83, column 2, first full paragraph) and states that "The topical antipsoriatic and anti-inflammatory profiles of EGF in experimental animal models suggest that this polypeptide may have a place in the medical management of human psoriasis" (see page 83, column 2 last paragraph). It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the EGF compositions of the Nanney et al article to treat psoriasis in human patients because the Casaco et al article teaches its successful use in treating psoriasis in animal models, and because the more animal models in which a drug can be successfully used, the more likely it is that the drug can be used in vivo in humans.

11. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being obvious over the Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301) in view of the Casaco et al article (Skin Pharmacol. Appl. Skin Physiol., Vol. 12, pages 79-84) as applied against claims 11-14 above, and further in view of the Phan et al article (Lancet, Vol. 348, page 547). The Nanney et al article suggests treating psoriasis in humans with EGF, but does not teach using the EGF in combination with sulfadiazine. The Phan et al article teaches treating a severe case of psoriasis using a combination of active ingredients including silver sulfadiazine 1% cream. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use a combination of the EGF of the Nanney et al article with the silver sulfadiazine 1% cream of the Phan et al article because it is prima facie obvious to use combinations of ingredients each of

which has been used individually for the same purpose (In re Kerkhoven, 205 USPQ 1069, 1072 (CCPA 1980)), because the Phan et al article teaches that it is known to use combinations of active ingredients in order to treat severe cases of psoriasis, and because combining the silver sulfadiazine of the Phan et al article with the EGF of the Nanney et al article would permit the EGF of the Nanney et al article to be used for the treatment of severe cases of psoriasis.

12. Claim 17 is rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 0 339 905. The European Patent Application '905 teaches the administration of growth factors, preferably EGF, for the treatment of wounds, including psoriasis. The EGF can be administered internally or topically, and its topical form includes creams. See, e.g., page 3, line 50 - page 4, line 8; page 4, lines 41-43; and Examples 1 and 2. The European Patent Application '905 does not specifically exemplify the treatment of psoriasis with EGF, and does not teach Applicant's claimed EGF concentrations. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to administer EGF either internally or topically in the treatment of psoriasis, because it is desirable in the art to be able to treat psoriasis and because the European Patent Application '905 teaches that psoriasis is a type of wound which growth factors such as EGF would have been expected to be useful in treating. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to determine all operable and optimal concentrations and dosages for the active agents of the European Patent Application '905 because drug concentration and dosage are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical arts.

13. Applicant's arguments filed August 28, 2003 have been fully considered but they are not persuasive.

The new Abstract did not address all of the objections set forth in the previous Office action and repeated above.

With respect to the objection to the specification for failure to provide proper antecedent basis for the claimed subject matter, it should be noted that this objection does not concern issues under 35 U.S.C. 112, first paragraph. The objection can be overcome by inserting verbatim into the specification the language which is found in Applicants' claims.

The Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301) is now relied upon under 35 U.S.C. 103(a) to reject Applicants' claims. The examiner agrees with Applicant that the Nanney et al article does not teach treating psoriasis in humans, but does not agree that the Nanney et al article does not suggest treating psoriasis in humans. Applicant contends that there is no model which would permit one of one ordinary skill in the art to extrapolate to in vivo results in human patients. The examiner disagrees, because the Nanney et al article's model uses actual human psoriatic lesions, and because the Nanney et al article describes its models as being excellent biological tools. Given that actual human psoriatic lesions are treated in the Nanney et al article, it is apparent that the Nanney et al article's model correlates to psoriasis in humans. Applicant has provided no evidence that there is no reasonable animal model in existence, and has provided no evidence that the particular animal model of the Nanney et al article is not reasonably predictive of in vivo human results. The Jackson et al article referred to by Applicant discusses animal or in vitro models of the factors involved in triggering and maintaining the chronic plaque of psoriasis; it does not discuss whether or not there exists an animal or in vitro

model for the treatment of psoriasis. As to Applicant's argument that "No other previous model could have removed all uncertainty about the use of EGF in psoriasis", prima facie obviousness does not require absolute certainty of success; rather, all that is required is a reasonable expectation of success. See MPEP 2143.02.

The obviousness rejection of claims 11-16 based upon the European Patent Application 0 339 905 is withdrawn in view of Applicant's new claim limitation requiring that EGF be the sole active agent. The European Patent Application '905 requires the use of a chemical entity which is capable of increasing the number of receptors for the growth factor on the membranes of cells at a wound site, e.g., a retinoid, and does not provide any motivation or suggest excluding such a chemical entity from its method of treatment. However, claim 17, which does not require treatment of a human patient, which does not require that the EGF be the sole active agent, and which does not require that the expression of EGF receptors be downregulated, remains rejected over the European Patent Application '905.

The obviousness rejection based upon the Nanney et al article (J. Invest. Dermatol., Vol. 98, pages 296-301), the Casaco et al article (Skin Pharmacol. Appl. Skin Physiol., Vol. 12, pages 79-84), and the Phan et al article (Lancet, Vol. 348, page 547) is maintained. Applicant has not shown that the invention satisfies a long felt need in the art by the submission of appropriate evidence in the form of an oath or declaration under 37 CFR 1.132, and Attorney's arguments do not satisfy the evidentiary requirements necessary for such a showing. See MPEP 716.01(c), second paragraph, and 716.04. There is motivation to combine the EGF of the Nanney et al article with the sulfadiazine of the Phen et al article for the reasons set forth in the rejection. The Phan et al article need not need not teach EGF or the combination of EGF and sulfadiazine in

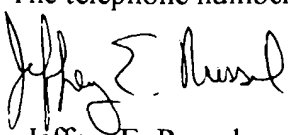
order for prima facie obviousness to be established; rather, it is the prior art when considered as a whole, and not just any single reference, which must be considered in determining whether or not prima facie obviousness exists.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
November 17, 2003